

contd.
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Cpd #	A	HetAr
5	[2-N(CH ₃) ₂ -5-CF ₃ CH ₂]pyrimidin-4-yl	2-(2,6-di-MeOPh)pyrimidin-5-yl
6	[2-N(CH ₃) ₂ -5-CF ₃ CH ₂]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyrazin-2-yl
7	[2-N(CH ₃) ₂ -5-(CH ₃) ₂ CH]pyrimidin-4-yl	2-(2,6-di-MeOPh)pyridin-5-yl
8	[2-N(CH ₃) ₂ -5-(CH ₃) ₂ CH]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyridin-2-yl
9	[2-N(CH ₃) ₂ -5-(CH ₃) ₂ CH]pyrimidin-4-yl	3-(2,6-di-MeOPh)pyridazin-6-yl
10	[2-N(CH ₃) ₂ -5-(CH ₃) ₂ CH]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyrimidin-2-yl
11	[2-N(CH ₃) ₂ -5-(CH ₃) ₂ CH]pyrimidin-4-yl	2-(2,6-di-MeOPh)pyrimidin-5-yl
12	[2-N(CH ₃) ₂ -5-(CH ₃) ₂ CH]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyrazin-2-yl
13	[2-N(CH ₃) ₂ -5-(CH ₃ CH ₂) ₂ CH]-pyrimidin-4-yl	2-(2,6-di-MeOPh)pyridin-5-yl
14	[2-N(CH ₃) ₂ -5-(CH ₃ CH ₂) ₂ CH]-pyrimidin-4-yl	5-(2,6-di-MeOPh)pyridin-2-yl
15	[2-N(CH ₃) ₂ -5-(CH ₃ CH ₂) ₂ CH]-pyrimidin-4-yl	3-(2,6-di-MeOPh)pyridazin-6-yl
16	[2-N(CH ₃) ₂ -5-(CH ₃ CH ₂) ₂ CH]-pyrimidin-4-yl	5-(2,6-di-MeOPh)pyrimidin-2-yl
17	[2-N(CH ₃) ₂ -5-(CH ₃ CH ₂) ₂ CH]-pyrimidin-4-yl	2-(2,6-di-MeOPh)pyrimidin-5-yl
18	[2-N(CH ₃) ₂ -5-(CH ₃ CH ₂) ₂ CH]-pyrimidin-4-yl	5-(2,6-di-MeOPh)pyrazin-2-yl
19	[2-N(CH ₃) ₂ -5-(3,5-di-CH ₃ isoxazol-4-yl)]pyrimidin-4-yl	2-(2,6-di-MeOPh)pyridin-5-yl
20	[2-N(CH ₃) ₂ -5-(3,5-di-CH ₃ isoxazol-4-yl)]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyridin-2-yl
21	[2-N(CH ₃) ₂ -5-(3,5-di-CH ₃ isoxazol-4-yl)]pyrimidin-4-yl	3-(2,6-di-MeOPh)pyridazin-6-yl
22	[2-N(CH ₃) ₂ -5-(3,5-di-CH ₃ isoxazol-4-yl)]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyrimidin-2-yl
23	[2-N(CH ₃) ₂ -5-(3,5-di-CH ₃ isoxazol-4-yl)]pyrimidin-4-yl	2-(2,6-di-MeOPh)pyrimidin-5-yl
24	[2-N(CH ₃) ₂ -5-(3,5-di-CH ₃ isoxazol-4-yl)]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyrazin-2-yl
25	[2-N(CH ₃) ₂ -5-(1,3,5-tri-CH ₃ pyrazol-4-yl)]pyrimidin-4-yl	2-(2,6-di-MeOPh)pyridin-5-yl
26	[2-N(CH ₃) ₂ -5-(1,3,5-tri-CH ₃ pyrazol-4-yl)]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyridin-2-yl
27	[2-N(CH ₃) ₂ -5-(1,3,5-tri-CH ₃ pyrazol-4-yl)]pyrimidin-4-yl	3-(2,6-di-MeOPh)pyridazin-6-yl
28	[2-N(CH ₃) ₂ -5-(1,3,5-tri-CH ₃ pyrazol-4-yl)]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyrimidin-2-yl

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Cpd #	A	HetAr
29	[2-N(CH ₃) ₂ -5-(1,3,5-tri-CH ₃ pyrazol-4-yl)]pyrimidin-4-yl	2-(2,6-di-MeOPh)pyrimidin-5-yl
30	[2-N(CH ₃) ₂ -5-(1,3,5-tri-CH ₃ pyrazol-4-yl)]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyrazin-2-yl
31	[2-N(CH ₃) ₂ -5-(3,5-di-CH ₃ isothiazol-4-yl)]pyrimidin-4-yl	2-(2,6-di-MeOPh)pyridin-5-yl
32	[2-N(CH ₃) ₂ -5-(3,5-di-CH ₃ isothiazol-4-yl)]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyridin-2-yl
33	[2-N(CH ₃) ₂ -5-(3,5-di-CH ₃ isothiazol-4-yl)]pyrimidin-4-yl	3-(2,6-di-MeOPh)pyridazin-6-yl
34	[2-N(CH ₃) ₂ -5-(3,5-di-CH ₃ isothiazol-4-yl)]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyrimidin-2-yl
35	[2-N(CH ₃) ₂ -5-(3,5-di-CH ₃ isothiazol-4-yl)]pyrimidin-4-yl	2-(2,6-di-MeOPh)pyrimidin-5-yl
36	[2-N(CH ₃) ₂ -5-(3,5-di-CH ₃ isothiazol-4-yl)]pyrimidin-4-yl	5-(2,6-di-MeOPh)pyrazin-2-yl

Please delete the paragraph starting on line 22 on Page 19 ✓

Please replace the paragraph starting on line 28 on Page 19 with the following paragraph: ✓

a² *N*-(2-(*N,N*-dimethylamino)-5-(2-isopropyl)pyrimidin-4-yl)-*L*-3-(2-(2,6-dimethoxyphenyl)pyridin-5-yl)alanine;

Please replace the paragraph starting on line 31 on Page 19 with the following paragraph: ✓

a³ *N*-(2-(*N,N*-dimethylamino)-5-(2-isopropylpyrimidin-4-yl)-*L*-3-(5-(2,6-dimethoxyphenyl)pyridin-2-yl)alanine;

Please replace the paragraph starting on line 34 on Page 19 with the following paragraph: ✓

a⁴ *N*-(2-(*N,N*-dimethylamino)-5-(2-isopropylpyrimidin-4-yl)-*L*-3-(3-(2,6-dimethoxyphenyl)pyridazin-6-yl)alanine;

Please replace the paragraph starting on line 1 on Page 20 with the following paragraph: ✓

a⁵ N-(2-(N,N-dimethylamino)-5-(2-isopropylpyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrimidin-2-yl)alanine;

The paragraph starting on line 4 on Page 20 with the following paragraph: ✓

a⁶ N-(2-(N,N-dimethylamino)-5-(2-isopropylpyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyrimidin-5-yl)alanine;

Please replace the paragraph starting on line 7 on Page 20 with the following paragraph: ✓

a⁷ N-(2-(N,N-dimethylamino)-5-(2-isopropylpyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrazin-2-yl)alanine;

Please replace the paragraph starting on line 22 on Page 21 with the following paragraph: ✓

a⁸ N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisothiazol-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyridin-2-yl)alanine;

Please replace the paragraph starting on line 25 on Page 21 with the following paragraph:

a⁹ N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisothiazol-4-yl)pyrimidin-4-yl)-L-3-(3-(2,6-dimethoxyphenyl)pyridazin-6-yl)alanine;

Please replace the paragraph starting on line 28 on Page 21 with the following paragraph: ✓

a¹⁰ N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisothiazol-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrimidin-2-yl)alanine;

Please replace the paragraph starting on line 31 on Page 21 with the following paragraph: ✓

a¹¹ N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisothiazol-4-yl)pyrimidin-4-yl)-L-3-(2-(2,6-dimethoxyphenyl)pyrimidin-5-yl)alanine; and

Please replace the paragraph starting on line 34 on Page 21 with the following paragraph: ✓

a¹² N-(2-(N,N-dimethylamino)-5-(3,5-dimethylisothiazol-4-yl)pyrimidin-4-yl)-L-3-(5-(2,6-dimethoxyphenyl)pyrazin-2-yl)alanine;

Please replace the paragraph starting on line 16 on Page 88 with the following paragraph: ✓

a¹³ A mixture of a heteroaryl halide or heteroaryl triflate (1.0 eq.), an arylboronic acid (1.1 eq.), CsCO₃ (1.5 eq.), Pd(PPh₃)₄ (0.03 eq.) And anhydrous DMF was stirred under nitrogen at 100°C for 48 h and then the DMF was evaporated. The residue was partitioned between ethyl acetate and half-saturated aqueous sodium chloride and then the ethyl acetate extracts were treated with magnesium sulfate, filtered and evaporated. The residue was purified by flash chromatography on silica gel using ethyl acetate/hexanes to give the heteroaryl-aryl product.

Please replace the paragraph starting on line 8 on Page 90 with the following paragraph: ✓

a¹⁴ The desired dipeptide ester was prepared by the reaction of a carboxylic acid (1 equivalent) with the appropriate amino acid ester or amino acid ester hydrochloride (1

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a¹⁴ equivalent), benzotriazol-1-yloxy-tris(dimethylamino)phos-phonium hexafluorophosphate [BOP] (2.0 equivalent), triethylamine (1.1 equivalent), and DMF. The reaction mixture was stirred at room temperature overnight. The crude product is purified by flash chromatography to afford the dipeptide ester.

Please replace the paragraph starting on line 2 on Page 104 with the following paragraph: ✓

a¹⁵ Synthesis of
N-(5-(2,2,2-trifluoroethyl)pyrimidin-4-yl)-D,L-3-(5-(2,6-dimethoxyphenyl)-
pyridin-2-yl)alanine

Please replace the paragraph starting on line 13 on Page 104 with the following paragraph: ✓

a¹⁶ 2,2,2-Trifluoroethyl triflate (prepared accordingly to Gassman, et al. J. Org. Chem., 1984, 49(12), 2258-2273) was converted via sequential application of methods Z, CC, and EE to give 4,6-dichloro-5-(2,2,2-trifluoroethyl)pyrimidine. D.L-(5-(2,6-dimethoxyphenyl)pyridine-2-yl)alanine ethyl ester and 4,6-dichloro-5-(2,2,2-trifluoroethyl)pyrimidine were coupled via method FF and the product was transformed via sequential application of methods GG and L to give the title compound.

Please replace the paragraph starting on line 1 on Page 105 with the following paragraph: ✓

a¹⁷ 2,2,2-Trifluoroethyl triflate (prepared accordingly to Gassman, et al. J. Org. Chem., 1984, 49(12), 2258-2273) was converted via sequential application of methods Z, CC, and EE to give 4,6-dichloro-5-(2,2,2-trifluoroethyl)pyrimidine. D.L-(5-(2-methoxyphenyl)pyridine-2-yl)alanine ethyl ester and 4,6-dichloro-5-(2,2,2-trifluoroethyl)pyrimidine were coupled via method FF and the product was transformed via sequential application of methods GG and L to give the title compound.